

Efficacy of Morphine Sulfate-Augmented Hepatobiliary Imaging in Acute Cholecystitis

Tony E. Vasquez, Daniel S. Rimkus, Mark G. Hass, and David I. LaRosa

Gould Medical Clinic, Modesto; and South Coast Nuclear Medicine, Santa Barbara, California

Objective: A review of the English language literature was performed to determine the sensitivity and specificity of morphine sulfate-augmented hepatobiliary imaging for acute cholecystitis. Twenty publications, involving 914 patients, were reviewed from journals published between 1984 and 1999. The analysis of these patients has resulted in the largest combined review study to date. The sensitivity and specificity of morphine-augmented hepatobiliary imaging were calculated to be 96.1% and 88.6%, respectively.

After reading this paper, the nuclear medicine technologist should be able to: (a) discuss the clinical use of morphine augmentation during hepatobiliary imaging; and (b) state the sensitivity and specificity of morphine sulfate-augmented hepatobiliary imaging.

Key Words: hepatobiliary imaging; acute cholecystitis; morphine sulfate; technetium-99m-IDA agents

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Since the introduction of ^{99m}Tc -N (2,6 dimethylphenylcarbonylmethyl) iminodiacetic acid (IDA) in 1975 by Loberg, Cooper, and Harvey, hepatobiliary imaging with IDA derivatives has become a routine method of evaluating the biliary system (1,2). Molecular changes of the benzene ring resulted in the synthesis of diisopropyl iminodiacetic acid. Technetium-99m disofenin and ^{99m}Tc -mebrofenin are widely used in the US for evaluating the hepatobiliary system (3,4).

The majority of patients having hepatobiliary examinations show prompt accumulation of the radiopharmaceutical in the liver, entry of tracer into the biliary tree and small intestine, and subsequent visualization of the gallbladder within 60 min of tracer administration. Acute cholecystitis is suggested by nonvisualization of the gallbladder (5). The gallbladder may not be visualized, however, despite normal excretion of radiopharmaceutical into the small intestine in various clinical settings, such as chronic cholecystitis (6,7), pancreatitis (8), total parenteral nutrition (9,10), alcoholism (9), hepatocellular disease (11), and prolonged fasting (10,12). Nonvisualization of the gallbladder at 60 min also may be a normal anatomic variant.

Morphine sulfate has been shown to reduce the incidence of nonvisualization of the gallbladder, improving the diagnostic accuracy of the test (13). This article evaluates the first 15 y of the use of morphine augmentation during hepatobiliary imaging for diagnosing acute cholecystitis.

MATERIALS AND METHODS

We reviewed peer-reviewed journals on the topic of morphine sulfate use during hepatobiliary imaging. An electronic literature search was conducted. The first publication involving the use of morphine sulfate during hepatobiliary imaging was in 1984 (14). Twenty publications between 1984 and 1999 were found that met the above criteria (13–32).

True positive (TP) was defined as a patient who had both nonvisualization of the gallbladder after morphine augmentation and a subsequent diagnosis of acute cholecystitis. True negative (TN) was defined as a patient who had both visualization of the gallbladder after morphine augmentation and did not have a subsequent diagnosis of acute cholecystitis. False positive (FP) was defined as a patient who had nonvisualization of the gallbladder after morphine augmentation and did not have a subsequent diagnosis of acute cholecystitis. False negative (FN) was defined as a patient who had visualization of the gallbladder after morphine augmentation and had a subsequent diagnosis of acute cholecystitis. The data from the 20 studies are compiled in Table 1.

DISCUSSION

The essential feature of acute cholecystitis is blockage of the cystic duct. In this instance, the purpose of cholescintigraphy is to evaluate cystic duct patency. Obstruction to gallbladder emptying increases bile concentration and chemical irritation of the gallbladder, which ultimately may result in acute cholecystitis (33). Stones occluding the cystic duct or the neck of the gallbladder are responsible for between 80–95% of the cases of acute cholecystitis (33,34).

Cholescintigraphy is an exquisitely sensitive test for determining the patency of the cystic duct. After excretion by the liver into small and large bile ducts, the radiopharmaceutical may transit the sphincter of Oddi into the duodenum or may flow

For correspondence or reprints contact: Tony E. Vasquez MD, RSO, Gould Medical Clinic, 600 Coffee Rd., Modesto, CA 95355; Phone: 209-524-1211.

TABLE 1
Results of Hepatobiliary Imaging with Morphine Sulfate Augmentation*

Reference	True positive	True negative	False positive	False negative	Others	Total
Choy, et al. (14)	23	12	0	1	0	36
Grund, et al. (15)	11	8	1	0	1	21
Kim, et al. (16)	18	18	4	0	0	40
Vasquez, et al. (13)	10	22	4	0	4	40
Olsen, et al. (17)	3	7	1	0	1	12
Mehta, et al. (18)	17	13	0	0	1	31
Lourides, et al. (19)	64	68	3	3	0	138
Flancbaum, et al. (20)	1	17	0	0	0	18
Flancbaum, et al. (21)	28	37	2	1	0	68
Fig, et al. (22)	15	22	10	1	0	48
Kistler, et al. (23)	13	14	4	1	0	32
Fink-Bennett, et al. (24)	35	23	1	2	0	61
Kim, et al. (25)	8	9	3	1	0	21
Kim, et al. (26)	24	15	4	2	0	45
Shapiro, et al. (27)	12	0	0	0	0	12
Flancbaum, et al. (28)	75	79	8	1	0	163
Flancbaum, et al. (29)	12	29	3	1	0	45
Yen, et al. (30)	15	14	0	1	0	30
Otes, et al. (31)	30	7	5	1	0	43
Kalliafas, et al. (32)	9	0	0	1	0	10
Totals	423	414	53	17	7	914

*The sensitivity of a procedure is used to describe the ability of a procedure to detect a disease when it is present. The sensitivity is calculated using the following equation:

$$\text{Sensitivity} = \text{TP}/(\text{TP} + \text{FN}) \times 100$$

$$\text{Sensitivity} = 423/(423 + 17) \times 100 = 96.1\%$$

The specificity of a procedure is used to describe the ability of a procedure to exclude a disease when it is not present. The specificity is calculated using the following equation:

$$\text{Specificity} = \text{TN}/(\text{TN} + \text{FP}) \times 100$$

$$\text{Specificity} = 414/(414 + 53) \times 100 = 88.6\%$$

through the cystic duct into the gallbladder. Constriction of the sphincter of Oddi by morphine sulfate administration retards emptying to the common bile duct, raises intraductal pressure, and promotes gallbladder filling if the cystic duct is patent (35,36).

A variety of physiologic and pathologic conditions has been demonstrated with nonvisualization of the gallbladder that may be falsely interpreted as suggesting acute cholecystitis. These include fasting more than 24 h before imaging, total parenteral alimentation, pancreatitis, alcoholism, hepatocellular disease, and chronic cholecystitis (6–12). The gallbladder may not be

seen in some normal patients until well past 1 h. The administration of morphine sulfate can reduce the incidence of false-positive results in patients undergoing hepatobiliary imaging for acute cholecystitis and who demonstrate transit of the radiopharmaceutical into the intestines without visualization of the gallbladder at 1 h.

CONCLUSION

Our review of the literature shows that the sensitivity of the hepatobiliary scan with morphine augmentation is 96.1% for acute cholecystitis. The specificity of the hepatobiliary scan with morphine augmentation is 88.6% for acute cholecystitis.

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